UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/981,087	05/27/98	ELMORE M	1581.0200000

HM22/1007

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EXAMINER	
WEATHERSPOON, J	

ART UNIT	PAPER NUMBER
1645	10

DATE MAILED: 10/07/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/981,087	Elmore et al
Examiner	**Group Art Unit**
John K. Weatherspoon	1645

☒ Responsive to communication(s) filed on *Sep 14, 1999* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-25* is/are pending in the application.

Of the above, claim(s) *13-18 and 25* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-12 and 19-24* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicants response dated 9/14/99, and election with traverse of Group I, claims 1-12 and 19-24, drawn to polypeptide free of botulinum toxin activity and polypeptide composition and vaccine comprising said polypeptide, has been entered into the record as Paper No. 9. Applicants traversal (page 1 of response) is on the ground(s) that the International Search Report and the holding of unity of invention indicate "that the two groups of claims lack the same or corresponding technical features." The examiner notes that applicants arguments for traversal are not persuasive because: as set forth in the restriction requirement dated 6/16/99, the two groups of claims do not relate to a single general inventive concept under PCT Rule 13.1 since, under PCT Rule 13.2, they lack the same or corresponding special technical features. As set forth previously, the expression "special technical feature" means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. Further, as set forth in the restriction requirement, while the instant claims all involve polypeptide free of botulinum toxin activity and free of toxoid which induce protective immunity to type F botulinum toxin, it is clear from East et al (Current Microbiology 29:69-77, 1994) that said polypeptide does not define a contribution over the prior art. East et al disclose sequence of a gene encoding for a nontoxic polypeptide component of botulinum type F (distinct from botulinum neurotoxin or BoNT). Thus for the reasons set forth in the previous restriction requirement, the restriction requirement is still deemed proper and is therefore made FINAL.

Claims 13-18 and 25 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

2. Acknowledgment is made of applicants claim for foreign priority based on application number 9511909.5 filed in Great Britain on 6/12/95. It is noted, however, that applicant has not filed a certified copy of said application as required by 35 U.S.C. 119(b).

Specification

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

4. Claim 19 is objected to because of the following informalities: line 2 of calim 19 recites "a polypeptide fee of", i.e. "fee" has an apparent misspelling. Appropriate correction is required.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1-7 and 9-10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Said claims are drawn to "a polypeptide" and

polypeptide composition comprising " a polypeptide" which reads on naturally occurring polypeptides as claimed, i.e. polypeptides that are not altered by the hand of man.

Claim Rejections - 35 USC § 112 first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Said claims are drawn to polypeptides "comprising...derivative of a heavy chain of a type F botulinum neurotoxin." One skilled in the art recognizes that the term "derivative" encompasses any modification(s) of an amino acid sequence, i.e. amino acid insertions, substitutions and/or deletions. However the specification provides insufficient guidance for one skilled in the art to predict the biological function, e.g. induction of protective immunity/eliciting an immunological response, of claimed polypeptides "comprising" any claimed "derivative," since any said modification(s) of an amino acid sequence makes determination of function unpredictable (see below). Protein chemistry is probably one of the most unpredictable areas of biotechnology (see the teachings of Lazar and Burgess, below) and that even a single amino acid substitution can alter biological function in an unpredictable manner. For example, replacement of a single lysine

residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al.). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduce the biological activity of the mitogen (see Lazar et al.). These references teach that the function of particular amino acids with regard to biological function, e.g. induction of protective immunity/eliciting an immunological response, is unpredictable a priori and thus one skilled in the art would be forced into undue experimentation in order to practice broadly the claimed invention. In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives encompassed in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice broadly the claimed invention. The specification does not support the broad scope of the claims which encompass a multitude of polypeptide derivatives because the specification does not disclose specific positions which can be predictably modified to produce functional immune responses as claimed, and provides essentially no guidance to which of the enormous possible choices of peptides is likely to be successful. Applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable

and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Claim Rejections - 35 USC § 112 second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 and dependent claims thereof, i.e. claims 6, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Said claims are indefinite for being in improper Markush format. The Office recommends the use of the phrase "selected from the group consisting of..." with the use of the conjunction "and" rather than "or" in listing the species. See MPEP 706.03(Y).

8. Claims 7-12 and 19-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms "a polypeptide adapted to facilitate or enhance purification of the composition" and "a polypeptide adapted to bind to a chromatography column" in said claims are relative terms which render the claims indefinite. The specification does not provide a standard for ascertaining the exact steps/elements required for claimed polypeptides to be "adapted," nor does the specification provide the requisite degree of "adaptation" required "to facilitate or enhance purification of the composition" or "to bind to a

chromatography column" as claimed, and one skilled in the art would not be reasonably apprised of the scope of the invention. Absent an exact definition of the term "adapted" the metes and bounds of said claims can not be ascertained.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-2, 12 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Sesardic et al (PCT Publication No. WO 94/21684, publication date 9/29/94). Sesardic et al disclose polypeptides free of "botulinum toxin activity and capable of priming a T cell to proliferate in response to a botulinum toxoid", vaccine comprising said polypeptides, and methods for vaccinating comprising administering said vaccine. Since said "botulinum toxoid" disclosed by Sesardic et al encompasses any botulinum toxoid, e.g. a type F botulinum toxin as claimed, further since the claims are drawn to vaccine and methods for vaccination, the limitations of said claims are anticipated by the prior art.

Status of Claims

10. No claim is allowed.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology center 1600, Group 1645 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1645 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Weatherspoon, Ph.D. whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached at (703) 308-3995.

John Weatherspoon, Ph.D.

September 29, 1999

Anthony Caputa, Ph.D.

Supervisory Primary Examiner

Group 1645